

### **REMARKS**

This submission is in response to the Office Action mailed March 17, 2009, for which a response is due on or before June 17, 2009, extendable to and including September 17, 2009. Applicant submits herewith a request for a two-month extension. Thus, the extended deadline for response is August 17, 2009. Accordingly, this Amendment is timely submitted.

Claims 1-18, 26-32, and 34-55 were pending in the instant application, of which claims 1-18 and 26-43 were withdrawn from consideration by the Examiner. Claims 1-18 and 26-43, previously withdrawn, and claim 56, previously pending, are hereby cancelled without prejudice. Claims 44-55 stand rejected. Claims 44-49, 52, 53, and 55 are hereby amended. Applicant submits that these amendments introduce no new matter.

### **Interview Summary**

Applicant would like to thank Examiner Packard for the courtesy of a telephonic interview with Applicant's undersigned representative on Friday, August 14, 2009. The claim rejections under 35 U.S.C., 112, were discussed along with the claim amendments submitted herewith. The claim rejections under 35 U.S.C., 103, also were discussed. In particular, the Carter *et al.* reference was discussed. The substance of the interview also is included in the following comments.

### **Rejections Under 35 U.S.C. 112, First Paragraph - Written Description**

In the Office Action, the Examiner rejected claim 44 under 35 U.S.C. 112, first paragraph, as allegedly lacking sufficient written description. The Examiner alleged that the subject specification does not provide a representative disclosure of TPEN derivatives and/or identifying characteristics that distinguish the claimed invention from other materials.

Applicant respectfully disagrees. The subject specification provides a large number of species of TPEN derivatives, which Applicant believes would have sufficiently described the claimed genus to one skilled in the art on the priority date of the present invention.

Nevertheless, in order to expedite prosecution, amended claim 44 is directed to TPEN and derivatives thereof selected from the group consisting of ethylenediamine, diethylenetriamine, triethylenetetramine, ethylenediamine, diethylenetriamine, triethylenetetramine, triethylenediamine, tetraethylenepentamine, aminoethylethanol amine, aminoethylpiperazine, pentaethylenhexamine, triethylenetetramine-hydrochloride, tetraethylenepentamine-hydrochloride, pentaethylenhexamine-hydrochloride, tetraethylpentamine, captopril, and penicillamine. Claim 56, rendered redundant by the amendment, is herein canceled.

The Examiner is thus respectfully requested to withdraw the rejection.

**Rejections Under 35 U.S.C. 112, First Paragraph - New Matter**

Further, the Examiner rejected claims 48 and 49 under 35 U.S.C. 112, first paragraph, for reciting selective prevention of capillary formation and inhibiting cancer spread by preventing capillary formation, which allegedly lacks sufficient support in the subject specification.

Applicant respectfully disagrees. The subject specification provides ample support for inhibition of angiogenesis using TPEN, *inter alia* in the following passage:

"Tumor expansion beyond microscopic size is angiogenesis dependent. TPEN was assessed for its ability to inhibit angiogenesis in an *in vitro* model. Bovine endothelial cells assemble into capillary like structures when seeded on Matrigel (FIG. 3, 0 nM of TPEN). This ability was impaired when TPEN was added to the medium, in a concentration dependent manner (FIG. 3, 1 nM-100 nM)" (paragraph [0045] of the pre-grant publication of the application as filed; emphasis added).

Nevertheless, in order to expedite prosecution, claims 48 and 49 have been amended to highlight their support in the application as filed.

The Examiner is thus respectfully requested to withdraw the rejection.

Further, the Examiner rejected claim 52 under 35 U.S.C. 112, first paragraph, for reciting enablement of normal physiological function, which allegedly lacks sufficient support in the subject specification.

Applicant respectfully disagrees. Applicant respectfully submits that the passage cited by the Examiner, paragraph 0050 of the pre-grant publication, provides ample support for enablement of normal physiological function:

Nevertheless, in order to expedite prosecution, claim 52 has been amended to highlight its support in the application as filed.

The Examiner is thus respectfully requested to withdraw the rejection.

**Rejections Under 35 U.S.C. 112, First Paragraph - Scope of Enablement**

Further, the Examiner rejected claims 44-54 under 35 U.S.C. 112, first paragraph, for allegedly lacking enablement commensurate with the scope of the claims. The Examiner alleged that the subject specification fails to provide sufficient enablement for preventing tumor cellular invasion or the diseases recited in claim 53. The Examiner admitted, however, that the subject specification enables reducing the risk of tumor cellular invasion and tumor metastasis.

Applicant agrees that the subject specification enables reducing the risk of tumor cellular invasion and tumor metastasis and respectfully disagrees with the rejection. Applicant respectfully submits that the striking inhibition of tumor cellular invasion and tumor metastasis shown in the subject specification (as shown *inter alia* in paragraph [0045] of the pre-grant publication of the application as filed) adequately supports a claim to preventing tumor cellular invasion.

Nevertheless, in order to expedite prosecution, claim 44 has been amended to cover subject matter agreed by Applicant and the Examiner to be amply supported in the subject specification. Amended claim 44 recites "inhibiting [as opposed to preventing] at least one of tumor cellular invasion and tumor metastasis." Amended claim 53 recites treatment, as opposed to prevention, of the recited diseases, and has further been amended to remove limitations already present in the main

claim. Support for the claim amendments is found throughout the subject specification, *inter alia* in paragraph [0038] of the pre-grant publication.

Accordingly, the amended claims cover subject matter agreed by the Examiner to be fully enabled. The Examiner is thus respectfully requested to withdraw the rejection.

**Rejections Under 35 U.S.C. 103(a)**

Further, the Examiner rejected claims 44-54 under 35 U.S.C. 103(a), as allegedly unpatentable over the Carter *et al.* reference in view of the Krajewska *et al.* reference. The Examiner alleged that Carter *et al.* taught depletion of intracellular  $Zn^{2+}$  using TPEN, increased lipid peroxidation in the apical cell membranes, activation of pro-caspase-3 and apoptosis, and that this reference relates to NCI-H292 cells, derived from metastasis of carcinoma. The Examiner admitted, however, that Carter does not teach the treatment of a mammal. The Examiner further alleged that Krajewska taught correlation between caspase-3 concentration and cell death in a variety of cell lines. The Examiner appears to conclude that a person of average skill in the art would somehow know to combine these two references and would somehow figure out, based on this combination, that TPEN can be used to treat metastasis of a pulmonary mucocypidermoid carcinoma.

Applicant agrees that Carter does not teach the treatment of a mammal and respectfully disagrees with the rejection. At the outset, Applicant would like to point out that Carter does not in any way teach or suggest use of TPEN as a therapeutic agent *for any purpose*. To the contrary, TPEN is used merely as an experimental tool to reduce  $Zn^{2+}$  levels. Krajewska does nothing to remedy the deficiencies of Carter and in fact does not in any way relate to TPEN. This point seems to be acknowledged by the Examiner in the assertion that that Carter did not teach the treatment of a mammal (page 10, first full paragraph). Thus, Applicant believes it would be exceedingly difficult to envisage any suggestion from these two references, either alone or in combination, of use of TPEN as a therapeutic agent *for any purpose*.

Further, Carter actually teaches against use of TPEN as an agent for treating metastasis, by the showing that TPEN induces caspases in primary sheep tracheobronchial AEC, similarly to the

immortalized cell lines tested. Thus, based on Carter, even if a person skilled in the art would believe TPEN to be pro-apoptotic, they would not consider it suitable for an anti-cancer agent, since it would indiscriminately kill both cancer cells and healthy cells. Krajewska does not in any way relate to TPEN and thus does nothing to remedy the deficiencies of Carter.

Further, Applicant respectfully points out to the Examiner that the subject claims are directed to inhibition of tumor cellular invasion and/or tumor metastasis. A method of treating a metastatic tumor by inducing apoptosis (which, as described hereinabove, is in any case not taught or suggested by the cited references) is not in any way relevant to inhibiting the process of tumor cellular invasion and/or the process of tumor metastasis. Krajewska does not in any way relate to TPEN and thus does nothing to remedy the deficiencies of Carter.

In summary, the references believed by the Examiner to be the closest prior art to the present invention fail to teach or suggest use of TPEN as for any therapeutic purpose, teach against use of TPEN as a selective anti-tumor agent, and do not relate in any way to inhibition of metastasis. Thus, the present invention is neither taught nor suggested in any way by the prior art.

Claims 44-49, 52-53, and 55 have been herein amended to ensure consistency with Examiner's instructions and add clarity to the invention. No new matter has been added. Therefore, and in view of the above amendments, Applicant believes the present application is in condition for allowance; notification of such is thus respectfully requested.

**CONCLUSION**

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, the Director is hereby authorized to charge any deficiency or credit any overpayment in the fees filed, asserted to be filed or which should have been filed herewith to our Deposit Account No. 23/2825, under Docket No. J0246.70000US00.

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Respectfully submitted,

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